Attorney Docket No. CFBF-P02-002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant(s):	Wagner et al.	Examiner:	P. Gambel
Serial No.:	08/948,393	Art Unit:	1644
Filing Date:	November 8, 1999		
For:	METHOD FOR TREATING AND PREVENTING ATHEROSCLEROSIS WITH PSGL-1		

CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

The undersigned hereby certifies that this document is being placed in the United States mail with first-class postage attached, addressed to the Commissioner for Patents, P.O. 1450 , Alexandria, VA. 22313-1450 on February 22, 2005.

Patricia McKenney

Commissioner for Patents
P.O. 1450
Alexandria, VA. 22313-1450

DECLARATION UNDER RULE 132

Sir:

I, Denisa D. Wagner, declare and state as follows:

1. I am a Professor in the Department of Pathology at Harvard Medical School, and a Senior Investigator at The CBR Institute for Biomedical Research, Inc., Boston, Massachusetts. My Curriculum Vitae is attached hereto as an Exhibit. I am also an inventor of the above-identified patent application. I consider myself to be an expert in the field of cardiovascular medicine and pathology, as reflected in my Curriculum Vitae, and I am well aware of the knowledge level of others skilled in this art.

2. I have reviewed the outstanding Office Action of October 21, 2004, in the above-identified patent application. I am also familiar with the claims of this application, as presently amended, which are directed to methods for treating or inhibiting atherosclerosis by decreasing the formation or growth of plaque on arterial walls. This is accomplished by administering PSGL-1, or selected variants thereof, to a subject over a prolonged period of time, i.e. months or years.

3. I am familiar with the references cited by the Examiner in the outstanding Office Action. In particular, I have reviewed the Cummings et al. reference (U.S. Patent No. 5,464,778), which I understand to be the primary reference cited in the Office Action.

4. The Cummings et al. reference is generally directed to inflammatory thrombotic conditions such as ischemia and reperfusion. In col. 19, line 64 to col. 20, line 5, the Cummings et al. reference makes the following disclosure relating to atherosclerosis and platelet-leukocyte interactions:

> "Platelet-leukocyte interactions are believed to be important in atherosclerosis. Platelets might have a role in recruitment of monocytes into atherosclerotic plaques; the accumulation of monocytes is known to be one of the earliest detectable events during atherogenesis. Rupture of a fully developed plaque may not only lead to platelet deposition and activation and the promotion of thrombus formation, but also the early recruitment of neutrophils to an area of ischemia."

5. My interpretation of the above cited passage is as follows. Cummings et al. speculate that platelet-leukocyte interactions are important in atherosclerosis. In fact, it is now well established that the key in atherosclerotic lesion development is the direct binding of monocytes to endothelial cells, and the reference does not discuss this. Cummings et al. discusses events following plaque rupture. Such events include thrombus formation leading to ischemic injury causing neutrophil recruitment. This event occurs long after plaque formation which is subject of the present application. The claims of our application specify that the P-selectin is on endothelial cells. Endothelial cells coat the arterial wall, and are not part of the

circulatory system as are the platelets. The plaque rupture, thrombotic events and neutrophil recruitment to the ischemic area discussed in the reference are not part of the present application.

6. I believe that the present invention can be distinguished from the Cummings et al. reference in the following respects. The present invention is directed to the treatment of atherosclerosis by decreasing the formation or growth of plaque on arterial walls. Atherosclerosis is a chronic condition caused by many factors, primarily by excessive plasma cholesterol levels, and results in the deposition of lesions and plaque on arterial walls. The treatment of atherosclerosis requires the long term administration of a medication to a subject in order to result in a meaningful improvement of the condition. This contrast with the treatment of a thrombosis, as disclosed in the Cummings et al. reference, which requires the commencement of an immediate treatment regime in order to prevent the reoccurrence of a thrombotic attack.

7. I also believe that the ability to design a mimetic of PSGL-1 having similar inhibitory characteristics, i.e. the ability to inhibit P-selectin, would be within the skill of a person in the art. Such a mimetic would optimally be designed based on a similarity of charge and shape as stated in the present claims.

8. Based on my knowledge, training and experience, it is my opinion that the references cited in the outstanding Office Action would not teach or suggest the method for treating atherosclerosis as stated in the present claims of the above-identified patent application.

I further declare that statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the above-identified application or any patent issuing thereon.

Date: 2/18/05

Denisa D. Wagner, Ph.D.

CURRICULUM VITAE

DENISA D. WAGNER, Ph.D.

ADDRESS: The CBR Institute for Biomedical Research
Harvard Medical School
800 Huntington Avenue
Boston, MA 02115
Phone: (617) 278-3344
FAX: (617) 278-3368

PLACE OF BIRTH: Prague, Czechoslovakia; U.S. citizen

EDUCATION: Universite de Geneve, Switzerland - Biochemistry
Diploma of Biochemistry, 1975, with distinction

Massachusetts Institute of Technology, Cambridge, MA
Biology - Ph.D., 1980

Harvard University, Cambridge, MA
M.A. (honorary), 1997

FACULTY POSITIONS:

Professor of Pathology, Harvard Medical School, Boston, MA.
1997-present.

Senior Investigator, The CBR Institute for Biomedical Research (formerly known as The Center for Blood Research), Boston, MA.
1994-present.

Associate Professor of Pathology, Harvard Medical School, Boston, MA.
1994-1997.

Associate Professor of Anatomy and Cellular Biology, Tufts University School of Medicine, Boston, MA. 1989-1994.

Associate Professor of Medicine, Tufts University School of Medicine and Member, Special and Scientific Staff, New England Medical Center, Boston, MA. 1987-1994.

Assistant Professor of Biophysics, University of Rochester School of Medicine and Dentistry, Rochester, New York. 1985-1987.

Assistant Professor of Medicine, University of Rochester School of Medicine and Dentistry, Rochester, New York. 1982-1987.

Senior Instructor in Medicine, University of Rochester School of Medicine and Dentistry, Rochester, New York. 1981-1982.

AWARDS:

Established Investigator Award, American Heart Association, Biosynthesis of von Willebrand protein by endothelial cells. 1986-1991.

XIth ISTH Congress award in recognition of an outstanding communication, 1987.

Gwendolyn J. Stewart Memorial Award to honor women in the biomedical sciences, 1998.

Special recognition award from the Council on Arteriosclerosis, Thrombosis and Vascular Biology, AHA, 1998

MERIT award, National Heart, Lung and Blood Institute, NIH, 1998-2008.

Sol Sherry Lecture, American Heart Association, 2004.

MAJOR COMMITTEE ASSIGNMENTS:

University:

1991-1994	Member of the Graduate Advisory Committee of the Graduate Program in Cell, Molecular and Developmental Biology, Sackler School of Graduate Biomedical Sciences, Tufts University
1992-1994	Sackler School Committee on Programs and Faculty, Tufts University
1992-1994	Graduate Admission Committee of the Graduate Program in Cell, Molecular and Developmental Biology, Sackler School of Graduate Biomedical Sciences, Tufts University
1995-Present	Member of the Graduate Program in Biological and Biomedical Sciences, Harvard Medical School
1998-Present	Member, Committee for Immunology, Program in Immunology, Harvard Medical School
1999-2002	Member of the Faculty Fellowship Committee, Harvard Medical School
2001-2004	Member, Standing Committee on Promotions, Reappointments, and Appointments, Harvard Medical School
2003-Present	Elected Member, Harvard Medical School Faculty Council

National and Regional:

Served on many review committees and panels for the National Institutes of Heath, American Heart Association, Juvenile Diabetes Foundation and American Red Cross.

Currently permanent member, NIH, NHLBI Thrombosis and Hemostasis Study Section (2002-2006)

MEMBERSHIPS, OFFICES, AND COMMITTEE ASSIGNMENTS IN PROFESSIONAL SOCIETIES:

1980-Present	American Society for Cell Biology
1982-Present	American Society of Hematology
1982-Present	International Society of Thrombosis and Haemostasis
1983-1997	Council on Thrombosis, American Heart Association
1985-Present	International Society of Thrombosis and Haemostasis, subcommittee on von Willebrand factor
1991-1996	American Heart Association, Vascular Wall Biology Study Committee

1992-Present	American Heart Association, Council on Thrombosis Executive Committee
1993-1995	American Heart Association, Council on Thrombosis Long-Range Planning Committee
1994-1996	American Heart Association, Council on Thrombosis Membership Committee (Chairman)
1994-Present	American Association for the Advancement of Science
1994-Present	North American Vascular Biology Organization (Founding Member)
1995-1998	American Society of Hematology, Scientific Subcommittee on Thrombosis & Vascular Biology
1997-Present	North American Vascular Biology Organization (Councilor)
1997-Present	Council on Arteriosclerosis, Thrombosis and Vascular Biology, American Heart Association (Fellow)
1998	Council of the Gordon Research Conferences (Member)
1998-Present	The Molecular Medicine Society (Member)
1999-Present	Boston Obesity Nutrition Research Center (Member)
2001-Present	National Hemophilia Foundation (Member)
2001-2005	American Society of Hematology, Scientific Committee on Thrombosis & Vascular Biology (Member)
2002-Present	Harvard Center for Neurodegeneration & Repair (Member)
2004-2010	Council of the International Society on Thrombosis and Haemostasis (Member)
2004-2005	Chair, Scientific Committee on Thrombosis and Vascular Biology, American Society of Hematology

EDITORIAL BOARDS:

1993-2004	Molecular Biology of the Cell
1994-1999	Journal of Clinical Investigation
1998-Present	Molecular Medicine
2003-2008	Blood

PUBLICATIONS
DENISA D. WAGNER, Ph.D.

1. Hynes RO, Ali IU, Destree AT, Mautner V, Perkins ME, Senger DR, **Wagner DD** and Smith KK. A large glycoprotein lost from the surfaces of transformed cells. Ann NY Acad Sci 312:317-342, 1978.

2. **Wagner DD** and Hynes RO. Domain structure of fibronectin and its relation to function (disulfides and sulfhydryl groups). J Biol Chem 254:6746-6754, 1979.

3. Hynes RO, Destree AT, Perkins ME and **Wagner DD.** Cell surface fibronectin and oncogenic transformation. J Supramolecular Str 11:95-104, 1979.

4. **Wagner DD** and Hynes RO. Topological arrangement of the major structural features of fibronectin. J Biol Chem 255:4304-4312, 1980.

5. **Wagner DD,** Ivatt R, Destree AT and Hynes RO. Similarities and differences between fibronectins of normal and transformed hamster cells. J Biol Chem 256:11708-11715, 1981.

6. **Wagner DD** and Hynes RO. Fibronectin coated beads are endocytosed by cells and align with microfilament bundles. Exp Cell Res 140:373-381, 1982.

7. Van De Water L III, **Wagner DD,** Crenshaw EB III and Hynes RO. Fibronectin-dependent endocytosis by macrophage-like ($P388D_1$) and fibroblastic (NIL 8) cells. In: Cellular Recognition. Glaser L, Frazier W and Gottlieb D (Eds.). New York: Alan R. Liss, 869-878, 1982.

8. Hynes RO, Destree AT and **Wagner DD.** Relationships between microfilaments, cell-substratum adhesion and fibronectin. Cold Spring Harbor Symposia on Quantitative Biology 46:659-669, 1982.

9. **Wagner DD,** Olmsted JB and Marder VJ. Immunolocalization of von Willebrand protein in Weibel-Palade bodies of human endothelial cells. J Cell Biol 95:355-360, 1982.

10. **Wagner DD** and Marder VJ. Biosynthesis of von Willebrand protein by human endothelial cells: identification of a large precursor polypeptide chain. J Biol Chem 258:2065-2067, 1983.

11. **Wagner DD,** Urban-Pickering M and Marder VJ. von Willebrand protein binds to extracellular matrices independently of collagen. Proc Natl Acad Sci USA 81:471-475. 1984.

12. Sporn LA, Rubin P, Marder VJ and **Wagner DD.** Irradiation induces release of von Willebrand protein from endothelial cells in culture. Blood 64:567-570, 1984.

13. **Wagner DD** and Marder VJ. Biosynthesis of von Willebrand protein by human endothelial cells: processing steps and their intracellular localization. J Cell Biol 99:2123-2130, 1984.

14. Sporn LA, Chavin SI, Marder VJ and **Wagner DD.** Biosynthesis of von Willebrand protein by human megakaryocytes. J Clin Invest 76:1102-1106, 1985.

15. **Wagner DD,** Mayadas T, Urban-Pickering M, Lewis BH and Marder VJ. Inhibition of disulfide bonding of von Willebrand protein by monensin results in small, functionally defective multimers. J Cell Biol 101:112-120, 1985.

16. Fay PJ, Kawai Y, **Wagner DD,** Ginsberg D, Bonthron D, Ohlsson-Wilhelm BM, Chavin SI, Abraham GN, Handin RI, Orkin SH, Montgomery RR and Marder VJ. Propolypeptide of von Willebrand factor circulates in blood and is identical to von Willebrand antigen II. Science 232:995-998, 1986.

17. Sporn LA, Marder VJ and **Wagner DD.** Inducible secretion of large biologically potent von Willebrand factor multimers. Cell 46:185-190, 1986.

18. **Wagner DD,** Mayadas T and Marder VJ. Initial glycosylation and acidic pH in the Golgi apparatus are required for multimerization of von Willebrand factor. J Cell Biol 102:1320-1324, 1986.

19. **Wagner DD,** Lawrence SO, Ohlsson-Wilhelm BM, Fay PJ and Marder VJ. Topology and order of formation of interchain disulfide bonds in von Willebrand factor. Blood 69:27-32, 1987.

20. **Wagner DD,** Fay PJ, Sporn LA, Sinha S, Lawrence SO and Marder VJ. Divergent fates of von Willebrand factor and its propolypeptide (von Willebrand antigen II) after secretion from endothelial cells. Proc Natl Acad Sci USA 84:1955-1959, 1987.

21. Sporn LA, Marder VJ and **Wagner DD.** von Willebrand factor released from Weibel-Palade bodies binds more avidly to extracellular matrix than that secreted constitutively. Blood 69:1531-1534, 1987.

22. Sinha S and **Wagner DD.** Intact microtubules are necessary for complete processing, storage and regulated secretion of von Willebrand factor by endothelial cells. Eur J Cell Biol 43:377-383, 1987.

23. Ribes JA, Francis CW and **Wagner DD.** Fibrin induces release of von Willebrand factor from endothelial cells. J Clin Invest 79:117-123, 1987.

24. Mayadas TN, **Wagner DD** and Simpson PJ. von Willebrand factor biosynthesis and partitioning between constitutive and regulated pathways of secretion after thrombin stimulation. Blood 73:706-711, 1989.

25. Handin RI and **Wagner DD.** von Willebrand factor: molecular and cellular biology. In: Progress in Hemostasis and Thrombosis (vol. 9). Coller B (Ed.). Philadelphia: W B Saunders, 233-259, 1989.

26. Roarke MC, **Wagner DD,** Marder VJ and Sporn LA. Temperature-sensitive steps in the secretory pathway for von Willebrand factor in endothelial cells. Eur J Cell Biol 48:337-343, 1989.

27. Sporn LA, Marder VJ and **Wagner DD.** Differing polarity of the constitutive and regulated secretory pathways for von Willebrand factor in endothelial cells. J Cell Biol 108:1283-1289, 1989.

28. Bonfanti R, Furie BC, Furie B and **Wagner DD.** PADGEM (GMP-140) is a component of Weibel-Palade bodies of human endothelial cells. Blood 73:1109-1112, 1989.

29. Avissar N, Whitin JC, Allen PZ, **Wagner DD,** Liegey P and Cohen HJ. Plasma selenium dependent glutathione peroxidase: cell of origin and secretion. J Biol Chem 264:15850-15855, 1989.

30. Ribes JA, Ni F, **Wagner DD** and Francis CW. Mediation of fibrin-induced release of von Willebrand factor from cultured endothelial cells by the fibrin β chain. J Clin Invest 1989, 84:435-442, 1989.

31. Mayadas TN and **Wagner DD.** In vitro multimerization of von Willebrand factor is triggered by low pH: importance of the propolypeptide and free sulfhydryls. J Biol Chem 264:13497-13503, 1989.

32. Larsen E, Celi A, Gilbert GE, Furie BC, Erban JK, Bonfanti R, **Wagner DD** and Furie B. PADGEM protein: a receptor that mediates the interaction of activated platelets with neutrophils and monocytes. Cell 59:305-312, 1989.

33. **Wagner DD.** Storage and secretion of von Willebrand factor. In: Role of Factor VIII and von Willebrand Factor. Zimmerman TS and Ruggeri ZM. (Eds.). New York: Marcel Dekker, pp. 161-180, 1989.

34. Larsen E, Palabrica T, Sajer S, Gilbert GE, **Wagner DD,** Furie BC and Furie B. PADGEM-dependent adhesion of activated platelets to monocytes and neutrophils is mediated by a lineage-specific carbohydrate, lacto-N-fucopentaose III (CD15). Cell 63:467-474, 1990.

35. **Wagner DD.** Cell biology of von Willebrand factor. In: Annual Review of Cell Biology. Palade GE, Alberts BM and Spudich JS. (Eds). 6:217-246, 1990.

36. Peters JH, Sporn LA, Ginsberg MH and **Wagner DD.** Human endothelial cells synthesize, process, and secrete fibronectin molecules bearing an alternatively spliced type III homology (ED1). Blood 75:1801-1808, 1990.

37. Mayadas TN and **Wagner DD.** von Willebrand factor biosynthesis and processing. Ann NY Acad Sci, 614:153-166, 1991.

38. Furie B, Celi A, Palabrica TM, Larsen E, **Wagner DD** and Furie, BC. PADGEM a Leukocyte Receptor on Activated Platelets: Biology and application to in vivo medical diagnostics. In: Biotechnology of Plasma Proteins: Haemostasis, Thrombosis and Iron Proteins. Albertini A, Lenfant CL, Mannucci PM, and Sixma JJ. (Eds). Basel: Karger, 32-36, 1991.

39. **Wagner DD** and Bonfanti R. von Willebrand factor and the endothelium. Mayo Clinic Proceedings 66:621-627, 1991.

40. Bevilacqua E, Butcher B, Furie B, Furie B, Gallatin M, Gimbrone M, Harlan J, Kishimoto K, Lasky L, McEver R, Paulson J, Rosen S, Seed B, Springer T, Stoolman L, Tedder T, Varki A, **Wagner DD**, Weissman I and Zimmerman G. Letter to the Editor. Selectins: A family of adhesion receptors. Cell 67:233, 1991.

41. **Wagner DD.** Structure and biology of von Willebrand factor. In: Hematology: Basic Principles and Practices. Benz EJ, Cohen HJ, Furie B, Hoffman R and Shattil SJ. (Eds.). New York: Churchill Livingstone, 1354-1358, 1991.

42. **Wagner DD,** Saffaripour S, Bonfanti R, Sadler JE, Cramer EM, Chapman B and Mayadas TN. Induction of specific storage organelles by von Willebrand factor propolypeptide. Cell 64:403-413, 1991.

43. Erban JK and **Wagner DD.** A 130 kDa protein on endothelial cells binds to amino acids 15-42 of the Bβ chain of fibrinogen. J Biol Chem 267:2451-2458, 1992.

44. Mayadas TN and **Wagner DD**. Vicinal cysteines in the prosequence play a role in von Willebrand factor multimer assembly. Proc Natl Acad Sci USA 89:3531-3535, 1992.

45. Larsen GR, Sako D, Ahern TJ, Shaffer M, Erban JK, Sajer SA, Gibson RM, **Wagner DD**, Furie BC and Furie B. P-Selectin and E-Selectin: Distinct but overlapping leukocyte ligand specificities. J Biol Chem 267:11104-11110, 1992.

46. Koedam JA, Cramer EM, Briend E, Furie B, Furie BC and **Wagner DD**. P-selectin, a granule membrane protein of platelets and endothelial cells, follows the regulated secretory pathway in AtT-20 cells. J Cell Biol 116:617-625,1992.

47. Stone JP and **Wagner DD**. P-selectin mediates adhesion of platelets to neuroblastoma and small cell lung cancer. J Clin Invest 92:804-813, 1993.

48. Vischer UM and **Wagner DD.** CD63 is a component of Weibel-Palade bodies of human endothelial cells. Blood 82:1184-1191, 1993.

49. Subramaniam M, Koedam JA and **Wagner DD**. Divergent fates of P- and E-selectins after their expression on the plasma membrane. Molec Biol of the Cell 4:791-801, 1993.

50. Journet AM, Saffaripour S and **Wagner DD**. Requirement for both D domains of the propolypeptide in von Willebrand factor multimerization and storage. Thromb Haemost 70:1053-1057,1993.

51. Mayadas TN, Johnson RC, Rayburn H, Hynes RO and **Wagner DD**. Leukocyte rolling and extravasation are severely compromised in P-selectin-deficient mice. Cell 74:541-554, 1993.

52. **Wagner DD.** Weibel-Palade body: The storage granule for von Willebrand factor and P-selectin. State of the Art book, Thromb Haemost 70:105-110, 1993.

53. Journet AM, Saffaripour S, Cramer EM, Tenza D, and **Wagner DD**. von Willebrand factor storage requires intact prosequence cleavage site. Eur J Cell Biol 60:31-41, 1993.

54. Vischer UM and **Wagner DD**. von Willebrand factor proteolytic processing and multimerization precede the formation of Weibel-Palade bodies. Blood 83:3536-3544, 1994.

55. **Wagner DD** and Hynes RO. Gene targeting of adhesion molecules in the vasculature. Series: Molecular genetics and gene therapy of cardiovascular diseases. Mockrin SC (Ed.) New York: Marcel Dekker, pp. 403-425, 1995.

56. Stone JP and **Wagner DD**. P-selectin-deficient mice: A model to study inflammation and metastasis. In: Series: Topics in Molecular Medicine Vol 1. Siess W, Lorenz R and Weber PC. (Eds.). New York: Raven Press, pp. 105-116, 1995.

57. **Wagner DD**. P-selectin knock-out: a mouse model for various human diseases. In: Cell adhesion and human disease. Ciba Foundation Symposium 189. Marsh J and Goode J (Eds). Chichester: John Wiley & Sons, pp. 2-16, 1995.

58. **Wagner DD** and Ginsburg D. Structure, biology and genetics of von Willebrand factor. In: Hematology: Basic Principles and Practices. 2nd Edition. Benz EJ, Cohen HJ, Furie B, Hoffman R and Shattil SJ. (Eds.). New York: Churchill Livingstone, 112:1717-1725, 1995.

59. Johnson RC, Mayadas TN, Frenette PS, Mebius RE, Subramaniam M, Lacasce A, Hynes RO and **Wagner DD**. Blood cell dynamics in P-selectin-deficient mice. Blood 86:1106-1114, 1995.

60. Subramaniam M, Saffaripour S, Watson SR, Mayadas TN, Hynes RO and **Wagner DD**. Reduced recruitment of inflammatory cells in a contact hypersensitivity response in P-selectin-deficient mice. J Exp Med 181:2277-2282, 1995.

61. **Wagner, DD**. P-selectin chases a butterfly. Editorial. J Clin Invest 95:1955-1956, 1995.

62. Frenette PS, Johnson RC, Hynes RO and **Wagner DD.** Platelets roll on stimulated endothelium *in vivo*: An interaction mediated by endothelial P-selectin. Proc Natl Acad Sci USA 92:7450-7454, 1995.

63. Yamada S, Mayadas TN, Yuan F, **Wagner DD,** Hynes RO, Melder RJ and Jain RK. Rolling in P-selectin deficient mice is reduced but not eliminated in the dorsal skin. Blood 86:3487-3492, 1995.

64. Pinsky DJ, Naka Y, Liao H, Oz MC, **Wagner DD**, Mayadas TN, Johnson RC, Hynes RO, Heath M, Lawson CA and Stern DM. Hypoxia-induced exocytosis of endothelial cell Weibel-Palade bodies: A mechanism for rapid neutrophil recruitment following cardiac preservation. J Clin Invest 97:493-500, 1996.

65. Mayadas TN, Mendrick DL, Brady HR, Tang T, Papayianni A, Assmann KJM, **Wagner DD**, Hynes RO and Cotran RS. Acute passive anti-glomerular basement membrane nephritis in P-selectin-deficient mice: Increased neutrophil influx and proteinuria and decreased lipoxin A_4 generation. Kidney Int 49:1342-1349,1996.

66. Subramaniam M, Frenette PS, Saffaripour S, Johnson RC, Hynes RO and **Wagner DD**. Defects in hemostasis in P-selectin-deficient mice. Blood 87:1238-1242, 1996.

67. Frenette PS, Mayadas TN, Rayburn H, Hynes RO and **Wagner DD**. Susceptibility to infection and altered hematopoiesis in mice deficient in both P-and E-selectins. Cell 84:563-574, 1996.

68. Tang T, Frenette PS, Hynes RO, **Wagner DD** and Mayadas TN. Cytokine-induced meningitis is dramatically attenuated in mice deficient in endothelial selectins. J Clin Invest 97:2485-2490, 1996.

69. Frenette PS and **Wagner DD**. Adhesion Molecules - Part 1. New Engl J Med 334:1526-1529, 1996.

70. Frenette PS and **Wagner DD**. Adhesion Molecules - Part II: Blood vessels and blood cells. New Engl J Med 335:43-45, 1996.

71. Hynes RO and **Wagner DD**. Genetic manipulation of vascular adhesion molecules in mice. J Clin Invest 98:2193-2195, 1996.

72. Johnson RC, Chapman SM, Dong ZM, Ordovas JM, Mayadas TN, Herz J, Hynes RO, Schaefer EJ and **Wagner DD**. Absence of P-selectin reduces fatty streak formation in mice. J Clin Invest 99:1037-1043, 1997.

73. Subramaniam M, Saffaripour S, Van De Water L, Frenette PS, Mayadas TN, Hynes RO and **Wagner DD.** Role of endothelial selectins in wound repair. Am J Path 150:1701-1709, 1997.

74. Frenette PS and **Wagner DD**. Insights into selectin function from knockout mice. Thromb Haemost, State-of-the-Art Issue, 78:60-64, 1997.

75. Dong ZM, Gutierrez-Ramos JC, Coxon A, Mayadas TN and **Wagner DD**. A new class of obesity genes encodes leukocyte adhesion receptors. Proc Natl Acad Sci USA 94:7526-7530, 1997.

76. Walter UM, Ayer LM, Wolitzky BA, **Wagner DD**, Hynes RO, Manning AM and Issekutz AC. Characterization of a novel adhesion function blocking monoclonal antibody to rat/mouse P-selectin generated in the P-selectin-deficient mouse. Hybridoma 16: 249-257, 1997.

77. Walter UM, Ayer LM, Manning AM, Frenette PS, **Wagner DD**, Hynes RO, Wolitzky BA and Issekutz AC. Generation and characterization of a novel adhesion function blocking monoclonal antibody recognizing both rat and mouse E-selectin. Hybridoma 16: 355-361, 1997.

78. Weiser MR, Pechet TTV, Williams JP, Ma M, Frenette PS, Moore FD, Kobzk L, Hynes RO, **Wagner DD**, Carroll MC and Hechtman HB. Experimental murine acid aspiration injury is mediated by neutrophils and the alternative complement pathway. J Appl Physiol 83:1090-1095, 1997.

79. Dong ZM and **Wagner DD**. Leukocytes fighting against obesity. Molecular Psychiatry 3:8-9, 1998.

80. Frenette PS, Moyna C, Hartwell DW, Lowe JB, Hynes RO and **Wagner DD.** Platelet-endothelial interactions in inflamed mesenteric venules. Blood 91:1318-1324, 1998.

81. de Mora F, Williams CMM, Frenette PS, **Wagner DD**, Hynes RO, and Galli SJ. P- and E-selectins are required for the leukocyte recruitment, but not the tissue swelling, associated with IgE- and mast cell-dependent inflammation in mouse skin. Laboratory Investigation 78:497-505, 1998.

82. Fleming JC, Berger G, Guichard J, Cramer EM, and **Wagner DD**. The transmembrane domain enhances granular targeting of P-selectin. Euro J Cell Biol 75:331-343, 1998.

83. Dong ZM, Chapman SM, Brown AA, Frenette PS, Hynes RO, and **Wagner DD**. The combined role of P- and E-selectins in atherosclerosis. J Clin Invest 102:145-152, 1998.

84. Denis C, Methia N, Frenette PS, Rayburn H, Ullman-Culleré M, Hynes RO, and **Wagner DD**. A mouse model of severe von Willebrand disease: Defects in hemostasis and thrombosis. Proc Natl Acad Sci USA 95:9524-9529, 1998.

85. Seiler KP, Ma Y, Weis JH, Frenette PS, Hynes RO, **Wagner DD**, and Weis JJ. E- and P-selectin are not required for resistance to severe murine Lyme arthritis. Infection and Immunity. 66:4557-2559, 1998.

86. Homeister JW, Zhang M, Frenette PS, Hynes RO, **Wagner DD**, Lowe JB, and Marks RM. Overlapping functions of E- and P-Selectin in neutrophil recruitment during acute inflammation. Blood. 92:2345-2352, 1998.

87. Hartwell D, Butterfield CE, Frenette PS, Kenyon BM, Hynes RO, Folkman J, and **Wagner DD**. Angiogenesis in P-and E-Selectin deficient mice. Microcirculation. 5:173-178, 1998.

88. Dong ZM and **Wagner DD**. Leukocyte-endothelial adhesion molecules in atherosclerosis. J Lab Clin Med 132:369-375, 1998.

89. Mazo IB, Gutierrez-Ramos JC, Frenette PS, Hynes RO, **Wagner DD**, and von Andrian UH. Hematopoietic progenitor cell rolling in bone marrow microvessels: Parallel contributions of endothelial selectins and VCAM-1. J Exp Med 18:465-474, 1998.

90. Berger G, Hartwell DW and **Wagner DD**. P-selectin and platelet clearance. Blood: 92:4446-4452, 1998.

91. Hartwell DW, Mayadas T, Frenette PS, Berger G, Rayburn H, Hynes RO and **Wagner DD**. Role of P-selectin cytoplasmic domain in granular targeting in vivo and in early inflammatory responses. J Cell Biol 143: 129-1141, 1998.

92. Frenette PS, Subbarao S, Mazo IB, von Andrian UH and **Wagner DD**. Endothelial selectins and VCAM-1 promote hematopoietic progenitor homing to bone marrow. Proc Natl Acad Sci USA 95:14423-14428, 1998.

93. Jia GQ, Gonzalo JA, Hidalgo A, **Wagner D**, Cybulsky M and Gutierrez-Ramos JC. Selective eosinophil transendothelial migration triggered by eotaxin via modulation of Mac-1/ICAM-1 and VLA4/VCAM-1 interactions. Int Immunol 11:1-10, 1999.

94. Shi C, Feinberg MW, Zhang D, Patel A, Sim CU, Dong ZM, Chapman SC, Gutierrez-Ramos JC, **Wagner DD**, Sibinga NES and Haber E. Donor MHC and Adhesion Molecules in Transplant Arteriosclerosis. J Clin Invest 103:469-474, 1999.

95. Soriano SG, Wang YF, **Wagner DD** and Frenette PS. P- and E-selectin -deficient mice are susceptible to cerebral ischemia-reperfusion injury. Brain Res 835:360-364, 1999.

96. Robinson SD, Frenette PS, Rayburn H, Cummiskey M, Ullman-Culleré M, **Wagner DD**, and Hynes RO, Multiple, targeted deficiencies in selectins reveal a predominant role for P-selectin in leukocyte recruitment. Proc Natl Acad Sci USA 96:11452-11457, 1999.

97. Enjyoji K, Sévigny J, Lin Y, Frenette PS, Christie PD, Schulte am Esch J, Imai M, Edelberg JM, Rayburn H, Lech M, Beeler DL, Csizmadia E, **Wagner DD**, Robson SC and Rosenberg RD. Targeted disruption of *cd39*/ATP diphosphohydrolase results in disordered hemostasis and thromboregulation. Nature Med 5: 1010-1017, 1999.

98. Hartwell, DW and **Wagner DD**. New discoveries with mice mutant in endothelial and platelet selectins. Thromb Haemost, State-of-the-Art Issue, 82:850-857, 1999.

99. Denis C and **Wagner DD**. Insights from von Willebrand disease animal models. Cell Mol Life Sci 56: 977-990, 1999.

100. Methia N, Denis C, and **Wagner DD**. Carboxypeptidase E does not mediate von Willebrand factor targeting to storage granules. Euro J Cell Biol 78:884-891, 1999.

101. Ginsburg D and **Wagner DD**. Structure, biology and genetics of von Willebrand factor. In: Hematology: Basic Principles and Practices. 3rd Edition. Hoffman R, Benz EJ, Shattil SJ, Furie B, Cohen HJ, Silberstein LE and McGlave P. (Eds.). New York: Churchill Livingstone, 1999.

102. Dong ZM, Brown AA and **Wagner DD**. The prominent role of P-selectin in the development of advanced atherosclerosis in ApoE-deficient mice. Circulation 101:2290-2295, 2000.

103. Frenette PS, Denis CV, Weiss L, Subbarao S, Hartwig JH, Vestweber D and **Wagner DD**. P-selectin glycoprotein ligand-1 (PSGL-1) is expressed on platelets and can mediate platelet-endothelial interactions in vivo. J Exp Med 191:1413-1422, 2000.

104. Ni H, Denis CV, Subbarao S, Degen JL, Sato TN, Hynes RO and **Wagner DD**. Persistence of platelet thrombus formation in arterioles of mice lacking both von Willebrand factor and fibrinogen. J Clin Invest 106:385-392, 2000.

105. Andre P, Denis CV, Ware J, Saffaripour S, Hynes RO, Ruggeri ZM and **Wagner DD**. Platelets adhere and translocate on von Willebrand factor presented by endothelium in stimulated veins. Blood 96:3322-3328, 2000.

106. Andre P, Hartwell D, Hrachovinova I, Saffaripour S and **Wagner DD**. Pro-coagulant state resulting from high levels of soluble P-selectin in blood. Proc Natl Acad Sci USA 97:13835-13840, 2000.

107. Denis CV, Kwack K, Saffaripour S, Maganti S, Andre P, Schaub RG and **Wagner DD**. Interleukin-11 significantly increases plasma von Willebrand factor and factor VIII in wild-type and von Willebrand disease mouse models. Blood 97:465-472, 2001.

108. Denis CV, André P, Saffaripour S and **Wagner DD**. Defect in regulated secretion of P-selectin leukocyte recruitment in von Willebrand factor-deficient mice. Proc Natl Acad Sci USA, 98:4072-4077, 2001.

109. Niederman R, Westernoff T, Lee C, Mark LL, Kawashima N, Ullman-Culler M, Dewhirst FE, Paster BJ, **Wagner DD**, Mayadas T, Hynes RO and Stashenko P. Infection-mediated early-onset periodontal disease in P/E-selectin-deficient mice. J Clin Periodontal 28:569-575, 2001.

110. Ni H, Ramakrishnan V, Ruggeri ZM, Papalia JM, Phillips DR and **Wagner DD**. Increased thrombogenesis and embolus formation in mice lacking glycoprotein V. Blood 98:368-373, 2001.

111. Methia N, André P, Denis CV, Economopoulos M and **Wagner DD.** Localized reduction of atherosclerosis in von Willebrand factor-deficient mice. Blood 98:1424-1428, 2001.

112. Methia N, André P, Hafezi-Moghadam A, Economopoulos M, Thomas KL and **Wagner DD**. ApoE deficiency compromises the blood brain barrier especially after injury. Mol Med 7:810-815, 2001.

113. Gotte M, Joussen AM, Klein C, Andre P, **Wagner DD**, Hinkes MT, Kirchhof B, Adamis AP, and Bernfield M. Role of syndecan-1 in leukocyte-endothelial interactions in the ocular vasculature. Invest Ophthalmol Vis Sci 43:1135-1141, 2002.

114. André P, Prasad KSS, Denis CV, He M, Papalia JM, Hynes RO, Phillips DR and **Wagner DD**. CD40L stabilizes arterial thrombi by a β3 integrin-dependent mechanism. Nature Med. 8:247-252, 2002.

115. Sethi S, Ziouzenkova O, Ni H, **Wagner DD**, Plutzky J and Mayadas TN. Oxidized omega-3 fatty acids in fish oil inhibit leukocyte-endothelial interactions through activation of PPARα. Blood 100:1340-1346, 2002.

116. Hoffmeister KM, Felbinger TW, Falet H, Denis CV, Bergmeier W, Mayadas TN, von Andrian UH, **Wagner DD**, Stossel TP and Hartwig JH. The clearance mechanism of chilled blood platelets. Cell 112: 87-97, 2003.

117. Ni H, Yuen PST, Papalia JM, Trevithick JE, Sakai T, Fässler R, Hynes RO and **Wagner DD**. Plasma fibonectin promotes thrombus growth and stability in injured arterioles. Proc Natl Acad Sci USA 100: 2415-2419, 2003.

118. Burger PC and **Wagner DD**. Platelet P-selectin facilitates atherosclerotic lesion development. Blood 101:2661-2666, 2003.

119. Italiano JE Jr, Bergmeier W, Tiwari S, Falet H, Hartwig JH, Hoffmeister K, André P, **Wagner DD** and Shivdasani RA. Mechanisms and implications of platelet discoid shape. Blood 101:4789-96, 2003.

120. Hrachovinova I, Cambien B, Hafezi-Moghadam A, Kappelmayer J, Camphausen RT, Widom A, Xia L, Kazazian HH Jr, Schaub RG, McEver RP and **Wagner DD**. P-selectin/PSGL-1 interaction generates microparticles that correct hemostasis in a murine model of hemophilia A. Nat Med 9:1020-1025, 2003.

121. Matsushita K, Morrell CN, Cambien B, Yang SX, Yamakuchi M, Bao C, Hara M, Quick RA, Cao W, O'Rourke B, Lowenstein JM, Pevsner J, **Wagner DD** and Lowenstein CJ. Nitric oxide regulates exocytosis by S-nitrosylation of N-ethylmaleimide-sensitive factor. Cell 115:1-20, 2003.

122. **Wagner DD.** Shear madness in TNF-α signaling. Blood 102:2711-2712, 2003.

123. Myers DD, Hawley AE, Farris DM, Wrobelski SK, Thanaporn P, Schaub RG, **Wagner DD**, Kumar A and Wakefield TW. P-selectin and leukocyte microparticles are associated with venous thrombogenesis. J Vasc Surg 38: 1075-1089, 2003.

124. Ni H, Papalia JM, Degen JL and **Wagner DD**. Control of thrombus embolization and fibronectin internalization by integrin αIIbβ3 engagement of the fibrinogen γ chain. Blood 102: 3609-3614, 2003.

125. Bergmeier W, Burger PC, Piffath CL, Hoffmeister KM, Hartwig JH, Nieswandt B and **Wagner DD**. Metalloproteinase inhibitors improve the recovery and hemostatic function of in vitro-aged or -injured mouse platelets. Blood 102: 4229-4235, 2003.

126. Cambien B, Bergmeier W, Saffaripour S, Mitchell HA and **Wagner DD**. Anti-thrombotic activity of TNF-α. J Clin Invest 112: 1589-1596, 2003.

127. **Wagner DD** and Burger PC. Platelets in inflammation and thrombosis. Arterioscler Thromb Vasc Biol 23: 2131-2137, 2003.

128. Cambien B and **Wagner DD**. A new role in hemostasis for the adhesion receptor P-selectin. Trends Mol Med 10: 179-186, 2004.

129. Bergmeier W, Rabie T, Strehl A, Piffath CL, Prostredna M, **Wagner DD** and Nieswandt B. GPVI down-regulation in murine platelets through metalloproteinase-dependent shedding. Thromb Haemost 91: 951-958. 2004.

130. Kondo T, Hafezi-Moghadam A, Thomas K, **Wagner DD** and Kahn CR. Mice lacking insulin or insulin-like growth factor 1 receptors in vascular endothelial cells maintain normal blood-brain barrier. Biochem Biophys Res Commun 317: 315-320, 2004.

131. Crittenden JR, Bergmeier W, Zhang Y, Piffath CL, Liang Y, **Wagner DD**, Housman DE and Graybiel AM. CalDAG-GEFI integrates signaling for platelet aggregation and thrombus formation. Nat Med 10: 982-986, 2004.

132. Bergmeier W, Piffath CL, Cheng G, Dole VS, Zhang Y, von Andrian UH and **Wagner DD**. Tumor necrosis factor-α-converting enzyme (ADAM17) mediates GPIbα shedding from platelets in vitro and in vivo. Circ Res 95: 677-683, 2004.

133. Ginsburg D and **Wagner DD**. Structure, biology and genetics of von Willebrand factor. In: Hematology: Basic Principles and Practices. 4th Edition. Hoffman R, Benz EJ, Shattil SJ, Furie B, Cohen HJ, Silberstein LE and McGlave P. (Eds.). New York: Churchill Livingstone, 2004.

134. Babic AM, Wang HW, Lai MJ, Daniels TG, Felbinger TW, Burger PC, Stricker-Krongrad A and **Wagner DD**. ICAM-1 and β2 integrin deficiency impairs fat oxidation and insulin metabolism during fasting. In press, Mol Med.

135. Wang, HW, Babic, AM, Mitchell HA, Liu K and **Wagner DD**. Elevated soluble ICAM-1 levels induce immune deficiency and increase adiposity in mice. In press, FASEB J.